REMARKS

Formal Matters

Claims 1 and 4 are pending in the application. New claims 39-45 are added to more particularly point out and distinctly claim Applicants' invention.

Claim 39 is added to more particularly point out and distinctly claim Applicants' invention which encompasses an isolated polypeptide comprising an EGF-like domain, wherein the EGF-like domain consists of an amino acid sequence having at least 75% amino acid sequence identity to SEQ ID NO:4, and wherein the amino acid sequence binds to ErbB4 receptor but not to ErbB2 receptor or ErbB3 receptor under experimentally comparable conditions and activates ErbB4 receptor tyrosine phosphorylation. Support for new claim 39 is found throughout the specification, such as in originally filed, now canceled claims 2 and 3; and at page 76, line 14 to page 83, line 12 (Examples 4 and 5).

Claims 40-45 are added to more particularly point out and distinctly claim Applicants' invention which encompasses a host cell expressing the polypeptide of claims 1, 4, and 39. Support for claims 40-45 is found throughout the specification, such as at page 10, lines 18-29; page 27, line 27 to page 28, line 3; page 29, lines 15-25; and page 36, line 4 to page 39, line 15.

No new matter is added by the amendments to the claims.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1 and 4 were rejected as indefinite because the phrase "the EGF-like domain of SEQ ID NO:4" allegedly lacks antecedent basis and the metes and bounds cannot be determined. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The phrase "the EGF-like domain of SEQ ID NO:4" does not lack antecedent basis because the EGF-like domain of NRG3 was discovered by Applicants to be SEQ ID NO:4. Thus, use of the word "the" to refer to "EGF-like domain" is appropriate based on the support provided in the specification. Withdrawal of the rejection under Section 112, second paragraph, based on an alleged lack of antecedent basis is respectfully requested.

The metes and bounds of the claims is readily understood based on the disclosure in the specification. Applicants discovered that SEQ ID NO:4 formed an EGF-like domain in NRG3. Use of the word "of" in the phrase "the EGF-like domain of SEQ ID NO:4" merely indicates this, as supporting recitations in the specification show, such as at page 16, line 29 to page 17, line 1 (legend for Fig. 5) and Fig. 5; page 19, lines 20-29, especially page 19, line 23-27; page 74, line 16-17; and Fig. 4A. Withdrawal of the rejection is respectfully requested.

It is also noted here and in the discussion that follows that Applicants' original disclosure further guides one of ordinary skill in the art to envision variant EGF-like domains capable of binding to the ErbB4 receptor. Claim 39 is added to capture that aspect of Applicants' invention.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1 and 4 were rejected because the metes and bounds of the EGF-like domain of the claims allegedly cannot be determined. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Applicants' arguments in the previous section apply to this rejection as well. In the previous section, Applicants pointed out that the metes and bounds of the EGF-like domain is readily understood to encompass SEQ ID NO:4 as indicated in claim 1 and

supported in the specification. Claim 39 is added to more particularly point out and distinctly claim embodiments of the invention which are polypeptides comprising an EGF-like domain, wherein the EGF-like domain consists of an amino acid sequence having at least 75% amino acid sequence identity to SEQ ID NO:4, and wherein the EGF-like domain has the binding characteristics of NRG3 as claimed.

The Examiner suggested in the Office Action at page 3 that the specification does not teach beyond the single EGF-like domain discovered by Applicants. Such is certainly not the case. In fact, Applicants carefully and adequately guide one of ordinary skill in the art to prepare and screen polypeptides of the claimed invention. Preparation of such polypeptides is described at, for example, page 40, line 12 to page 47, line 29 (conservative and non-conservative amino acid substitutions described at page 41, line 18 to page 42, line 12, as well as insertion and deletion mutations described at page 42, line 13 to page 43, line 27; site-directed mutagenesis described at page 45, line 9 to page 46, line 3; PCR mutagenesis described at page 46, lines 4-24; cassette mutagenesis described at page 46, lines 25-26; mutagenesis by phagemid display method described at page 46, line 27 to page 47, line 29)). Peptide analogs are described at page 64, line 20 to page 65, line 3. Cloning methods are described at, for example, page 72, line 1 to page 73, line 19. Screening methods are described at, for example, page 66, lines 2-5 (for activation of cell growth, proliferation and differentiation in ErbB4 expressing cells); page 73, line 21 to page 74, line 26 (Example 2, characterization of deduced amino acid sequence); page 75, line 28 to page 76, line 12 (Example 3, expression analysis); page 76, lien 14 to page 83, line 12 (Examples 4 and 5, characterization of binding and tyrosine activation); page 83, line 14 to page 85, line 15 (Example 6,

cellular proliferation analysis); and in Figs. 1-7. This extensive guidance allows one of ordinary skill in the art to predictably prepare, isolate, and screen polypeptides of the invention. Thus, one of ordinary skill in the art is readily enabled by Applicants' disclosure to practice the claimed invention.

Applicants submit that the rejection with respect to enablement has been overcome and respectfully request withdrawal of the rejection.

Claims 1 and 4 were rejected as allegedly containing subject matter not described in the specification in such a way as to convey that Applicants were in possession of the claimed invention at the time of filing. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims.

Each claim as a whole encompasses a polypeptide comprising an EGF-like domain of SEQ ID NO:4. Claim 39 further encompasses polypeptides comprising an EGF-like domain consisting of an amino acid sequence having 75% amino acid sequence identity to SEQ ID NO:4, and having the binding characteristics of NRG3 as claimed. The Examiner suggests on page 5 of the Office Action that the claims are drawn to a large genus. The size of the genus is not an issue, however, if as here the members of the genus can be envisioned by one of ordinary skill in the art. The term, "polypeptide," does not present a written description problem because this term is sufficiently specific for one of ordinary skill in the art to readily envision members of the claimed genus when the ordinarily skilled artisan's knowledge is coupled with Applicants' disclosure. In addition, the terms "EGF-like domain" and SEQ ID NO:4 are described throughout the specification, including at the recitations listed above in this Response, such

that members of the genus can be envisioned. Finally, EGF-like domains having at least 75% amino acid identity to SEQ ID NO:4 and conferring the binding characteristics of NRG3 as claimed are described in the originally filed specification, such as at page 31, lines 14-18 and in original claim 3, as well as throughout the specification as recited in earlier paragraphs of this Response with respect to enablement. Thus, taken as a whole, the claims are supported by written description of each member of the genus, thereby allowing each member to be readily envisioned by the ordinarily skilled artisan in possession of Applicants' disclosure.

Applicants respectfully submit that the rejection under Section 112, first paragraph, has been overcome and respectfully request withdrawal of the rejection.

The rejections having been overcome, allowance of the claims is respectfully requested.

SUMMARY

Claims 1 and 4 are pending in the application. New claims 39-45 are added. The rejections are overcome by Applicants pointing out that Applicants' original disclosure coupled with ordinary skill in the art renders the claims definite with respect to what is meant by the EGF-like domain of SEQ ID NO:4. Similarly, the claims are enabled by the extensive description of routine procedures for preparing and screening members of the claimed genera. Finally, the originally filed disclosure indicates that Applicants were in possession of the claimed subject matter on the priority date because one of ordinary skill in the art can readily envision members of the claimed genera.

If the Examiner believes a telephone conference would expedite the prosecution of this application, the Examiner is

invited to call the undersigned at the number indicated below.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**."

This response is timely submitted with a transmittal letter and petition and fees for a one-month extension of time. In the unlikely event that these documents are separated from this response or if a one-month extension of time is insufficient to maintain pendency of the application, Applicants hereby petition the Commissioner to authorize charging our Deposit Account 07-0630 for any fees required or credits due and any extensions of time necessary to maintain the pendency of this application.

Respectfully submitted,
GENENTECH, INC.

Date: April 11, 2001 By: _____

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CLAIMS: Version with markings to show changes made

New Claims:

-39. An isolated polypeptide comprising an EGF-like domain, wherein the EGF-like domain consists of an amino acid sequence having at least 75% amino acid sequence identity to SEQ ID NO:4, and wherein the EGF-like domain has the binding characteristics of NRG3 comprising:

(a) binding to ErbB4 receptor but not to ErbB2 receptor or ErbB3 receptor under experimentally comparable conditions; and

(b) activation of ErbB4 receptor tyrosine phosphorylation.

40. A host cell expressing the polypeptide of claim 1.

41. The host cell of claim 40, wherein the host cell is selected from the group consisting of a mammalian cell, a yeast cell, an insect cell, a plant cell, a lower eukaryote, and a prokaryote.

42. A host cell expressing the polypeptide of claim 4.

43. The host cell of claim 42, wherein the host cell is selected from the group consisting of a mammalian cell, a yeast cell, an insect cell, a plant cell, a lower eukaryote, and a prokaryote.

44. A host cell expressing the polypeptide of claim 39.

45. The host cell of claim 44, wherein the host cell is selected from the group consisting of a mammalian cell, a yeast cell, an insect cell, a plant cell, a lower eukaryote, and a prokaryote.--